

Remarks

Reconsideration of this Application is respectfully requested.

Upon entry of the foregoing amendment, claims 42-102 are pending in the application, with claims 42, 48, 58, 64, 69, 75, 85, and 91 being the independent claims. Claims 1-41 are sought to be cancelled without prejudice to or disclaimer of the subject matter therein. Claims 42-102 are sought to be added. These changes are believed to introduce no new matter, and their entry is respectfully requested.

Based on the above amendment and the following remarks, Applicants respectfully request that the Examiner reconsider all outstanding objections and rejections and that they be withdrawn.

Support for New Claims

Support for new claims 42-44 can be found throughout the specification, and specifically in original claims 1, 4, and 5, respectively. Support for new claims 48-54 can be found throughout the specification, and specifically in original claims 6 and 9-14, respectively. Support for new claims 58-60 can be found throughout the specification, and specifically in original claims 15, 18, and 19, respectively. Support for new claims 64 and 65 can be found throughout the specification, and specifically in original claims 20 and 21, respectively. Support for new claims 69-71 can be found throughout the specification, and specifically in original claims 22, 25, and 26, respectively. Support for new claims 75-81 can be found throughout the specification, and specifically in original claims 27-33, respectively. Support for new claims 85-87 can be found throughout the specification, and

specifically in original claims 34, 35 and 36, respectively. Support for new claims 91-93 can be found throughout the specification, and specifically in original claims 37, 38 and 41, respectively. Support for new claims 45-47, 55-57, 61-63, 66-68, 72-74, 82-84, 88-90, and 94-96 can be found in the specification, *inter alia*, at page 10, lines 14-21. Support for new claims 43, 49, 59, 65, 70, and 93 can also be found, *inter alia*, in the specification at page 14, lines 21-23. Support for new claims 97-102 can be found in the specification, *inter alia*, at page 6, line 25 through page 7, line 3.

Oath/Declaration

The Examiner stated that the previously-submitted declaration is defective. In response, Applicants submit herewith a substitute declaration.

Claim Objections

The Examiner objected to claims 5 and 8 for grammatical informalities. Claims 5 and 8 have been cancelled. None of the newly added claims contain the inadvertent errors found in original claims 5 and 8. Thus, the Examiner's objections are rendered moot and should be withdrawn.

Rejections under 35 USC § 101

Claim 1 is rejected under 35 USC § 101 as being directed to non-statutory subject matter. *See* Paper No. 6, page 3. The Examiner asserted that claim 1 reads on naturally occurring microorganisms and noted that products of nature are not patentable. *See id.* According to the Examiner, amending the claim to read "An isolated rapid growing

microorganism. . ." would overcome the rejection. Applicants respectfully traverse this rejection.

Nevertheless, Applicants have cancelled claim 1. New claim 42 is similar to original claim 1, however, new claim 42 recites an *isolated* rapid growing *E. coli* lacking endogenous plasmids. Therefore, the rejection of claim 1 under 35 USC § 101 should be withdrawn and would not apply to new claim 42.

Rejections under 35 U.S.C. § 112, First Paragraph

Claims 1, 2, 6, 7, 11, 14-16, 20, 22, 23, and 27-39 are rejected under 35 USC § 112, first paragraph, on the ground that:

the specification, while being enabling for the rapidly growing strains of *E. coli* listed in Table I, does not reasonably provide enablement for **any** rapidly growing microorganism. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Paper No. 6, page 4 (emphasis in original).

The Examiner concluded that "it would clearly require undue experimentation by one of skill in the art to use any rapid growing microorganism in the claimed cloning and/or protein expression methods." Paper No. 6, page 6. In support of this conclusion, the Examiner provided an analysis of the factors relating to undue experimentation as set forth in *In re Wands*, 858 F.2d 731, 8 USPQ2d 1400 (Fed. Cir. 1988). Applicants respectfully traverse the rejection.

Nevertheless, solely to expedite prosecution, Applicants have cancelled claims 1, 2, 6, 7, 11, 14-16, 20, 22, 23, and 27-39. The claims added in their place are all directed to *E.*

coli (or to methods, kits or compositions requiring *E. coli*). Thus, the Examiner's rejection under 35 USC § 112, first paragraph, should be withdrawn and would not apply to any of the newly added claims.

Rejections under 35 U.S.C. § 112, Second Paragraph

Claims 1-41 are rejected under 35 USC § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. *See* Paper No. 6, page 7. According to the Examiner, "[t]he term 'rapid growing' is not defined by the claims, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention." *Id.* The Examiner acknowledged that the specification defines a rapid growing microorganism as having a growth rate of 5% - 200% increased as compared to a reference microorganism. Nevertheless, the Examiner contended that "[t]here is no definitive reference microorganism nor is there defined culture conditions for ascertaining increased growth of a microorganism." *Id.* Based on this analysis, the Examiner stated that any microorganism can be considered rapid growing. Applicants respectfully traverse the rejection.

Applicants have cancelled claims 1-41. The newly added claims, however, also include the term "rapid growing." Applicants contend that the term "rapid growing" is clearly defined in the specification as a microorganism that grows more rapidly than strains typically used in molecular biology applications. *See* specification at page 10, lines 14-16. Rapid growing microorganisms, including rapid growing *E. coli*, are identified on the basis of their growth rate as compared to a reference microorganism. *See id.* at page 10, lines 16-

22. Relative growth rate can be ascertained, *e.g.*, on the basis of colony size or doubling time. *See id.* at page 15, lines 3-11. The reference microorganisms contemplated within the scope of the claims include *E. coli* MM294 (ATCC33625) as well as DH5 α , DH10B, and "any other strain routinely used in cloning applications." *Id.* at page 10, lines 22-25. Finally, the culture conditions necessary to practice the claimed invention were known by, or readily available to, those skilled in the art at the time the application was filed. *See id.* at page 15, lines 6-10.

Thus, it would be clear to one of ordinary skill in the art what is meant by the term "rapid growing" as this term is used in both the original and newly added claims. More particularly, the skilled artisan, based on Applicants' disclosure, would understand that not *any* organism can be considered rapid growing -- only those microorganisms that exhibit a faster growth rate as compared with a reference microorganism (as that term is clearly defined in the specification) can be regarded as "rapid growing" within the scope of the present claims. Therefore, the term "rapid growing" does not render Applicants' claims indefinite. Accordingly, the rejection under 35 USC § 112, second paragraph, should be withdrawn and would not apply to any of the newly added claims.

Rejections under 35 U.S.C. § 102

Khosla et al.

Claim 1 is rejected under 35 USC § 102(b) as being anticipated by Khosla *et al.*, *Mol. Microbiol.* 6:3237-3249 (1992) ("Khosla"). *See* Paper No. 6, page 8. According to the Examiner, "Khosla *et al.* disclose a strain of bacteria, *Streptomyces coelicolor*, that is a rapid

growing microorganism lacking endogenous plasmids." *Id.* Applicants respectfully traverse the rejection.

Claim 1 has been canceled. New claim 42 is similar to claim 1, however, new claim 42 is directed to isolated rapid growing *E. coli* lacking endogenous plasmids. Khosla does not anticipate new claim 42 (or any other newly added claim) because Khosla does not disclose *E. coli*. Accordingly, the Examiner's rejection under 35 USC § 102(b) based on Khosla should be withdrawn and would not apply to Applicants' newly added claims.

Bharathi et al.

Claims 1-3 and 20 are rejected under 35 USC § 102(b) as being anticipated by Bharathi *et al.* *FEMS Microbiol. Lett.* 84:37-40 (1991) ("Bharathi"). *See* Paper No. 6, page 8. According to the Examiner, Bharathi discloses a (rapid growing) strain of *E. coli* lacking endogenous plasmids and methods for making said strain. *See id.* Applicants respectfully traverse the rejection.

Claims 1-3 and 20 have been cancelled. New claim 42 is similar to claim 1, however, new claim 42 is directed to isolated rapid growing *E. coli* lacking endogenous plasmids. New claim 64 is similar to claim 20, however, new claim 64 is directed to a method of producing an *E. coli* for cloning comprising (a) obtaining rapid growing *E. coli* having endogenous plasmids; and (b) curing said rapid growing *E. coli* of endogenous plasmids.

Bharathi describes a comparative study of the susceptibility of broad-host range *E. coli* vector plasmids to various curing agents. *See* Bharathi at page 37, column 1. Bharathi does not anticipate Applicants' original or newly added claims because the *E. coli* strains disclosed in Bharathi are not rapid growing; that is, there is no evidence presented indicating

that the Bharathi strains grow faster than a "reference microorganism" as this term is defined in the specification. In fact, the Bharathi reference does not even specify the full genotype of the *E. coli* strains used in the experiments. Nor is there a citation in Bharathi directing the skilled artisan to a source where one could look to ascertain the genotype of the strains¹. In view of the experiments described in Bharathi (determining the curing activity of various agents on broad-host range vector plasmids in *E. coli*), one must conclude that the strains used therein are among those commonly used in molecular biology applications; *i.e.*, they are not "rapid growing."

Because the Bharathi strains are not "rapid growing," none of Applicants original or newly added claims (including, in particular, new claims 42 and 61) read on these strains. Accordingly, the Examiner's rejection under 35 USC § 102(b) based on Bharathi should be withdrawn and would not apply to Applicants' newly added claims.

U.S. Patent No. 4,966,841 to Riley

Claims 6-8, 11, and 22-24 are rejected under 35 USC § 102(b) as being anticipated by U.S. Patent No. 4,966,841 to Riley ("Riley"). *See* Paper No. 6, page 9. According to the Examiner, "Riley discloses a method of cloning enhancer fragments comprising the steps of constructing a population of recombinant cloning vectors, transforming an *Escherichia coli* host strain with the recombinant cloning vectors and selecting the transformed *Escherichia coli* cells containing the recombinant vector." *Id.* Applicants respectfully traverse the rejection.

¹The paragraph bridging pages 37 and 38 in Bharathi merely indicates that the *E. coli* cultures used in the experiments were obtained from the Institute of Microbial Technology in Chandigarh, India. There is no discussion of the growth rates of the strains relative to a reference microorganism.

The basis for the rejection is the Examiner's assumption that "[t]he *E. coli* strain selected by Riley is considered to be capable of rapid growth." Paper No. 6, page 9. In support of this assumption, the Examiner cites the following passage in Riley:

The recombinant DNA plasmids, as prepared above, are used to transform host cells. The host cells may be any appropriate prokaryotic or eukaryotic cell. For example, the host may be composed of a well-defined bacteria, such as *E. coli* or a yeast strain. Such hosts are readily transformed and *capable of rapid growth* and culture.

Riley at column 6, lines 12-18 (emphasis added).

Claims 6-8, 11, and 22-24 have been cancelled. New claim 48 is similar to original claim 6, however, new claim 48 is directed to a method of cloning comprising the steps of (a) obtaining competent *E. coli*; (b) transforming said *E. coli* with at least one vector; (c) selecting transformed *E. coli* containing said at least one vector; and (d) culturing said transformed *E. coli*, wherein said cultured *E. coli* are rapid growing *E. coli*. New claim 69 is similar to original claim 22, however, new claim 69 is directed to a method of transforming rapid growing *E. coli*, comprising the steps of (a) obtaining competent *E. coli*; (b) incubating said competent *E. coli* in the presence of one or more vectors under conditions which cause said one or more vectors to be taken up by the *E. coli*; and (c) culturing said *E. coli*, wherein said cultured *E. coli* are rapid growing *E. coli*.

The microorganisms described in Riley do not possess the characteristics that would render them "rapid growing;" *i.e.*, these strains do not grow more rapidly than microorganisms typically used in molecular biology applications. The microorganisms described in Riley include the commercially available strains of *E. coli*., MM294, RR1, HB101, DH1 and JM107. *See* Riley at column 6, lines 24-26. Since these *are* strains that

are themselves "currently used for biotechnology applications," it follows that they cannot be regarded as "rapid growing" within the bounds of this term as used in the present claims. Therefore, neither the original claims nor the new claims read on the methods and strains set forth in Riley. Accordingly, the Examiner's rejection under 35 USC § 102(b) based on Riley should be withdrawn and would not apply to Applicants' newly added claims.

Bhandari et al.

Claims 15-17 are rejected under 35 USC § 102(b) as being anticipated by Bhandari *et al. J. Bacteriol.* 179:4403-4406 (1997) ("Bhandari"). *See* Paper No. 6, page 9. According to the Examiner, Bhandari discloses a method of producing a protein by transforming *E. coli* cells with a recombinant vector carrying a gene for the protein. *See id.* Again, the rejection is based on the assumption that "*E. coli* is considered to be a microorganism capable of rapid growth." *See id.* Applicants respectfully traverse the rejection.

Claims 15-17 have been cancelled. New claim 58 is similar to original claim 15, however, new claim 58 is directed to a method of producing a protein or peptide, comprising the steps of (a) obtaining competent *E. coli*; (b) transforming into said *E. coli* a vector containing a gene encoding a protein or peptide; and (c) culturing said transformed *E. coli* under conditions that cause said transformed *E. coli* to produce said protein or peptide, wherein said cultured *E. coli* are rapid growing *E. coli*.

There is no indication or suggestion that the *E. coli* strains in Bhandari are "rapid growing." That is, there is no evidence that the Bhandari strains grow more rapidly than those microorganisms currently used for biotechnology applications. In fact, the *E. coli* strains disclosed in Bhandari are derived from the commonly used strain BL21(DE3) and therefore are properly regarded themselves as "strains routinely used in cloning

applications." *See* Bhandari at page 4403, column 1. Therefore, neither the original claims nor the new claims read on the methods and strains set forth in Bhandari. Accordingly, the Examiner's rejection under 35 USC § 102(b) based on Bhandari should be withdrawn and would not apply to Applicants' newly added claims.

U.S. Patent No. 4,981,797 to Jessee et al.

Claims 34-37, 39 and 40 are rejected under 35 USC § 102(b) as being anticipated by U.S. Patent No. 4,981,797 to Jessee *et al.* ("Jessee"). *See* Paper No. 6, page 10. According to the Examiner, Jessee discloses a composition comprising rapid growing microorganisms as well as a method of making competent *E. coli*. *See id.* The rejection is apparently based on the Examiner's assumption that the *E. coli* strains of Jessee are "rapid growing microorganisms." Applicants respectfully traverse the rejection.

Claims 34-37, 39 and 40 have been cancelled. New claims 85, 86 and 87 are similar to original claims 34-36, respectively, however, new claims 85, 86 and 87 are directed to compositions comprising rapid growing *E. coli*. New claim 91 is similar to original claims 37, 39 and 40, however, new claim 91 is directed to a method of making competent rapid growing *E. coli*.

Jessee teaches four specific strains of *E. coli*: RR1, HB101, DH1, and DH5. These strains are all strains that are routinely used in cloning applications and are therefore not "rapid growing." Therefore, neither the original claims nor the new claims read on the methods and strains set forth in Jessee. Accordingly, the Examiner's rejection under 35 USC § 102(b) based on Jessee should be withdrawn and would not apply to Applicants' newly added claims.

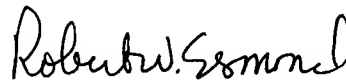
Conclusion

All of the stated grounds of objection and rejection have been properly traversed, accommodated, or rendered moot. Applicants therefore respectfully request that the Examiner reconsider all presently outstanding objections and rejections and that they be withdrawn. Applicants believe that a full and complete reply has been made to the outstanding Office Action and, as such, the present application is in condition for allowance. If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

Prompt and favorable consideration of this Amendment and Reply is respectfully requested.

Respectfully submitted,

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Date: Nov. 21, 2001

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